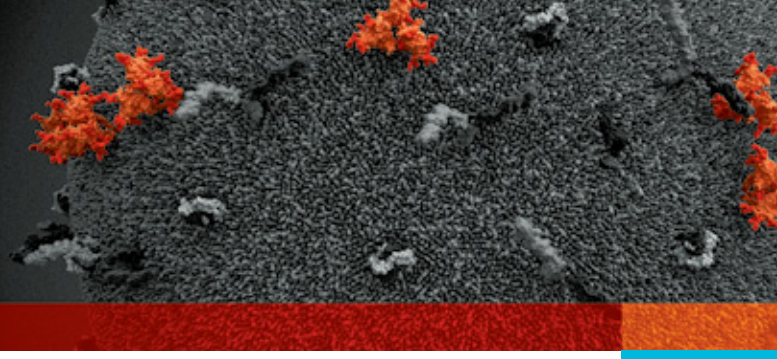

ABOUT THE NATIONAL INSTITUTES OF HEALTH (NIH)

What is the NIH?

The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, is the primary Federal agency conducting and supporting medical research. The NIH is the world's leading funder of basic, preclinical, clinical, behavioral, and translational research overall, and of HIV/AIDS research in particular.

From its beginning as a one-room laboratory in 1887, the NIH today comprises 27 Institutes and Centers each with a specific research agenda, often focusing on particular diseases or body systems, that investigate the causes of and ways to prevent, treat, and cure disease. The NIH conducts research in its own laboratories (intramural research) and awards peer-reviewed research grants and contracts to, and supports the training of, scientists at universities, medical schools, hospitals, and research institutions in every U.S. state and throughout the world (extramural research).

Nearly 6,000 scientists work in NIH intramural laboratories, and at the world's largest clinical research hospital, the NIH Clinical Center. Intramural research, however, is only 10 percent of the NIH's work. More than 83 percent of NIH funding supports critical research conducted beyond the NIH campus. The NIH's extramural research programs support the critical work of more than 300,000 personnel at some 3,000 universities, medical schools, and other institutions in every U.S. state and throughout the world.

Successful biomedical research depends on the talent and dedication of the scientific workforce. The NIH supports many innovative training programs and funding mechanisms that foster scientific creativity and exploration. The goal is to strengthen our nation's research capacity, broaden our research base, and inspire a passion for science in current and future generations of researchers.

The NIH encourages and depends on public involvement in federally supported research and activities. The NIH's wide-ranging public efforts include outreach and education, requests for public input on NIH projects, and special programs designed specifically to involve public representatives in clinical research.

For more information about the NIH and its programs, please visit *http://www.nih.gov.*

Where is the NIH located?

The NIH is headquartered in Bethesda, Maryland, United States, just outside Washington, DC. The NIH also has several facilities across the United States and abroad, including facilities in the Rockville, Maryland, area, and the National Cancer Institute Frederick Cancer Research and Development Center at Fort Detrick in Frederick, Maryland. The National Institute of Environmental Health Sciences main facility is located in Research Triangle Park, North Carolina.

Other laboratory facilities include the NIH Animal Center in Poolesville, Maryland; the National Institute on Aging Gerontology Research Center in Baltimore, Maryland; the Division of Intramural Research of the National Institute on Drug Abuse, also in Baltimore; the National Institute of Allergy and Infectious Diseases Rocky Mountain Laboratories in Hamilton, Montana, and several smaller field stations.

What are the NIH's major research accomplishments?

NIH research has supported virtually every significant biomedical advance in the past 50 years, including:

- The development of vaccines to protect against cervical cancer, pneumonia, flu, shingles, and meningitis
- Major decreases in deaths from heart disease, stroke, and many forms of cancer
- Advances in the diagnosis and care of Alzheimer's disease, Parkinson's disease, diabetes, asthma, depression, addiction, arthritis, and autism
- The development of targeted drug therapies that save lives with fewer side effects
- Advances against major diseases of the developing world, such as cholera and rotavirus
- Advances in the fields of genetic research and individualized medicine
- Stem cell research to study neurological disorders such as Parkinson's, Huntington's, amyotrophic lateral sclerosis (ALS), and spinal cord injury.

More than 130 Nobel Prize winners have received support from the NIH. Their studies have led to the development of magnetic resonance imaging (MRI), understanding of how viruses can cause cancer, insights into cholesterol control, and knowledge of how our brain processes visual information, among dozens of other advances.

In the field of HIV, NIH AIDS research has resulted in landmark advances that have led to:

- Co-discovery of HIV, the virus that causes AIDS
- Development of the first blood test for the disease, which has allowed diagnosis of infection as well as ensured the safety of the blood supply
- Establishment of the scientific basis for antiretroviral therapy, development or co-development of several key anti-HIV drugs, and extensive assessment of the best uses of HIV therapies and multidrug regimens that have saved more than 14 million years of life around the world
- Development of treatments for many HIV-associated coinfections, comorbidities, malignancies, and clinical manifestations, with benefits for patients also suffering from those other diseases
- Groundbreaking strategies for the prevention of mother-to-child transmission, which have resulted in dramatic decreases in perinatal HIV in the United States
- Demonstration that the use of male circumcision can reduce the risk of HIV acquisition
- The first step in proving the concept that a vaccine to prevent HIV infection is feasible; and discovery of two potent human antibodies that can stop more than 90 percent of known global HIV strains from infecting human cells in the laboratory
- Demonstration of the first proof of concept for the feasibility of a microbicide gel capable of preventing HIV transmission
- Demonstration that the use of therapy by infected individuals can dramatically reduce transmission to an uninfected partner
- Demonstration of the potential feasibility of pre-exposure prophylaxis, that long-term use of antiretroviral treatment regimens by some high-risk uninfected individuals can reduce risk of HIV acquisition
- Discovery that genetic variants may play a role in protecting some individuals, known as "elite controllers," who have been exposed to HIV over an extended period, from developing symptoms and enabling them to control the infection without therapy
- Critical basic science discoveries that continue to provide the foundation for novel research
- Progress in both basic and treatment research efforts aimed at eliminating viral reservoirs in the body, which, for the first time, is leading scientists to design and conduct research aimed at a cure.

What are the major components of the NIH?

The Office of the Director is the central office at the NIH, responsible for setting NIH policy and for planning, managing, and coordinating the programs and activities of all the NIH components. The NIH Director is responsible for providing leadership to the Institutes and for constantly identifying needs and opportunities, especially for efforts that involve multiple Institutes.

The NIH includes 27 research Institutes and Centers, including the NIH Clinical Center, the world's largest clinical research hospital. As HIV/AIDS transcends every area of clinical medicine and basic scientific investigation, the NIH AIDS research effort involves every NIH Institute and Center.

The Office of AIDS Research (OAR), located in the Office of the NIH Director, has primary responsibility for planning and coordinating AIDS research across the Institutes and Centers. Through its annual comprehensive trans-NIH planning, budgeting, and portfolio assessment processes, OAR sets scientific priorities, enhances collaboration, and ensures that research dollars are invested in the highest priority areas of scientific opportunity that will lead to new tools in the global fight against AIDS.

The NIH Institutes and Centers include the:

National Cancer Institute (NCI)

National Eye Institute (NEI)

National Heart, Lung, and Blood Institute (NHLBI)

National Human Genome Research Institute (NHGRI)

National Institute on Aging (NIA)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

National Institute of Allergy and Infectious Diseases (NIAID)

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

National Institute on Deafness and Other Communication Disorders (NIDCD)

National Institute of Dental and Craniofacial Research (NIDCR)

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

National Institute on Drug Abuse (NIDA)

National Institute of Environmental Health Sciences (NIEHS)

National Institute of General Medical Sciences (NIGMS)

National Institute of Mental Health (NIMH)

National Institute on Minority Health and Health Disparities (NIMHD)

National Institute of Neurological Disorders and Stroke (NINDS)

National Institute of Nursing Research (NINR)

National Library of Medicine (NLM)

Center for Information Technology (CIT)

Center for Scientific Review (CSR)

Fogarty International Center (FIC)

National Center for Complementary and Alternative Medicine (NCCAM)

National Center for Advancing Translational Sciences (NCATS)

NIH Clinical Center (CC)

For more information, see *http://www.nih.gov/icd.*

What is the NIH Intramural Research Program?

The Intramural Research Program (IRP) is the internal research program of the NIH. With 1,200 principal investigators and more than 4,000 postdoctoral fellows in basic, translational, and clinical research, the IRP is the largest biomedical research institution in the world. Known for its synergistic approach to biomedical science, the IRP is an expanse of highly productive Federal laboratories with an emphasis on high-risk, high-reward research designed to maximize the scope and impact of NIH basic research accomplishments on the practice of medicine and improvements in public health.

The unique funding environment of the IRP facilitates opportunities to conduct both long-term and high-impact science that otherwise would be difficult to undertake.

With rigorous external reviews ensuring that only the most outstanding research secures funding, the IRP is responsible for many scientific accomplishments, including the discovery of fluoride to prevent tooth decay, the use of lithium to manage bipolar disorder, and the creation of vaccines against hepatitis, *Haemophilus influenzae* (HIB), and human papillomavirus (HPV).

Clinical trials have been a key feature of the IRP portfolio. The program excels in the type of basic research needed to advance biomedical knowledge, providing the foundation for health research worldwide, as well as the type of clinical research that culminates in cures and therapies.

Clinical trials performed in the IRP are distinct. Some have tested research concepts so nascent that no scientific literature existed that could support a traditional grant application. In other cases, the advances arose from years of basic and clinical research only made possible by the equipment, expertise, and research freedom available in the IRP. For example, the National Cancer Institute (NCI) Center for Cancer Research (CCR) has developed a novel vaccine technology which, in turn, has led to the first FDA-approved vaccine against cancer. CCR partnered with private industry to create two vaccines against certain cancerous strains of HPV, which could help to prevent most cases of cervical cancer, as well as genital warts and other types of genital cancer. The NCI Division of Cancer Epidemiology and Genetics continues this work with a Phase III clinical trial in Costa Rica that is testing the safety and efficacy of one of these vaccines against specific deadly strains of HPV. The vaccine likely will have its major impact on the prevention of cervical cancer in developing nations, as well as in underserved populations within the United States.

Information about the NIH Intramural Research Program can be found at *http://irp.nih.gov*.

What is the NIH Clinical Center?

Opened in 1953 and located on the main NIH campus, the NIH Clinical Center is the world's largest clinical research hospital, and an important part of the NIH Intramural Research Program (IRP).

The NIH Clinical Center works to rapidly translate scientific observations and laboratory discoveries into new approaches for diagnosing, treating, and preventing disease. Research at the Clinical Center has led to advances in the development of chemotherapy for cancer; the first use of an immunotoxin to treat a malignancy; identification of the genes that cause kidney cancer and the development of new, targeted treatments for advanced kidney cancer; advances in depression treatment; the first gene therapy; the first treatment for AIDS; and the development of tests to detect HIV and hepatitis viruses in blood, which led to a safer blood supply.

Currently, about 1,500 clinical research studies are in progress at the NIH Clinical Center. Many focus on rare diseases, which often are not studied anywhere else. Most other studies are clinical trials, predominantly Phase I and Phase II studies, which often are the first tests of new drugs and therapies in people. The Clinical Center sees 10,000 new research participants a year, and more than 400,000 clinical research participants from every U.S. state and around the world have been active partners in discovery there to date.

Some 1,200 physicians, dentists, and Ph.D. researchers; 620 nurses; and 450 allied health care personnel work at the NIH Clinical Center. The collaborative environment of the NIH Clinical Center makes it possible for investigators to make referrals for immediate testing and confer with peers across research interests to identify the best approach for diagnosing and treating patients.

Learn more about IRP clinical trials by visiting the NIH Clinical Research Trials and You Web site at *http://www.nih.gov/health/clinicaltrials*.

To search for a specific IRP clinical trial, visit the NIH Clinical Trials Database at *http://clinicalstudies.info.nih.gov*.

Facilities to support patients at the Clinical Center include The Children's Inn, open 365 days a year; a school teaching kindergarten through high school for young patients; and the Edmond J. Safra Family Lodge for families and loved ones of adult patients. Other programs of the NIH Clinical Center include a range of clinical research training to help prepare the next generation of clinician-scientists.

For more information about the Clinical Center, visit *http://clinicalcenter.nih.gov/ccc/crc*.

What is the Vaccine Research Center?

Another key component of the NIH Intramural Research Program is the Dale and Betty Bumpers Vaccine Research Center (VRC), a part of the National Institute of Allergy and Infectious Diseases. The mission of the VRC is to conduct research that facilitates the development of effective vaccines for human disease. The primary research focus is the development of vaccines for AIDS, but the VRC also is working on vaccines for other diseases, including Ebola, Marburg, and influenza.

Activities in the VRC include:

- Basic research to establish mechanisms of inducing long-lasting protective immunity against HIV and other pathogens that present special challenges to vaccine development
- The conception, design, and preparation of vaccine candidates for HIV and related viruses
- Laboratory analysis, animal testing, and clinical trials of such candidates.

The VRC conducts a comprehensive program of research on the NIH intramural campus and works with scientists in academic, clinical, and industrial laboratories through a program of national and international collaborations. The VRC seeks industrial partners for the development, efficacy testing, and marketing of vaccines, and focuses the development of new methodologies and training opportunities that will benefit all HIV vaccine researchers. The potential scientific advances, methodologies, and resources also will provide the basis for research on vaccines for other diseases.

What is the NIH Extramural Research Program?

More than 83 percent of NIH funding supports extramural research—critical research conducted off the NIH campus. NIH-supported extramural research is conducted by more than 300,000 personnel at some 3,000 universities, medical schools, and other institutions in every U.S. state and throughout the world. Extramural research grants are competitively awarded based on a dual-level, peer-review process to new and early-stage investigators, as well as to experienced investigators for highly meritorious applications. The NIH offers a variety of research training and career development awards. Small business research funding opportunities and contract funding opportunities also are available through the NIH Extramural Research Program.

Information about NIH grants can be found at *http://grants.nih.gov/grants/about_grants.htm*.

The *NIH Guide for Grants and Contracts*, the official publication for NIH medical and behavioral research grant policies, guidelines, and funding opportunities, can be accessed at *http://grants.nih.gov/grants/guide/index.html*.

The NIH awards financial support in the form of grants, cooperative agreements, and contracts. This assistance supports the advancement of the NIH mission of enhancing health, extending healthy life, and reducing the burdens of illness and disability. While the NIH awards many grants specifically for research, it also provides grant opportunities that support

research-related activities, including: fellowships and training, career development, scientific conferences, resources, and construction.

The types of research grants, career development awards, program projects and center grants, resource grants, and research training and fellowships supported by the NIH can be found at: *http://grants.nih.gov/grants/funding/funding_program.htm.*

Information about the grants process specific to non-U.S. applicants/grantees can be found at *http://grants.nih.gov/grants/foreign/special_guidance.htm.*

What kinds of research training programs does the NIH support?

The NIH supports a wide variety of individual and institutional training grants and fellowships, including the Ruth L. Kirschstein National Research Service Award, career development awards, and extramural loan repayment programs.

NIH-funded HIV/AIDS research is a global endeavor. To facilitate a truly global AIDS research program, the NIH supports the training of domestic and international AIDS researchers; the development of research infrastructure such as equipment, shared instrumentation, and tissue and specimen repositories in many locations, including resource-limited settings in Africa, the Caribbean, India, and Asia; and capacity building for the conduct of AIDS-related research, including preclinical and clinical studies in many resource-limited settings throughout the world.

The Fogarty International Center Division of International Training and Research administers research grants, training grants, and fellowship programs at sites in more than 100 countries. Fogarty programs that build the research pipeline are anchored to peer-reviewed research grants and designed to be collaborative, long-term, and flexible. Nearly a quarter of Fogarty awards are made directly to robust research institutions in the developing world. The remaining grants support scientists at U.S. institutions who collaborate with colleagues abroad. About one-third of Fogarty's grants focus on scientific discovery, and two-thirds support research training.

NIH-funded programs also recruit individuals from underrepresented populations into research careers and support the development of research infrastructure at minority-serving institutions in the United States.

The NIH supports the NIH AIDS Research Loan Repayment Program and the Intramural AIDS Research Fellowship Program, which help ensure an adequate number of trained AIDS researchers at the NIH. Information about NIH training and career development opportunities can be found at *http://grants.nih.gov/training.*

Each NIH Institute and Center provides information about its training and research career opportunities at *http://grants.nih.gov/training/trainingfunds.htm.*

Information about the many training opportunities within the NIH intramural program, including programs for college students, recent college graduates, graduate students, medical and dental students, and postdoctoral candidates, can be found at *https://www.training.nih.gov/programs.*

What is peer review?

NIH research grants are awarded through a rigorous and highly competitive dual-level, peer-review process that supports the most promising and innovative approaches to pressing medical challenges facing the United States and the world. Applications submitted to the NIH for grants or cooperative agreements to support biomedical and behavioral research are evaluated for scientific and technical merit. NIH policy is intended to ensure that grant applications submitted to the NIH are evaluated on the basis of a process that is fair, equitable, timely, and free of bias.

The first level of review is carried out by a Scientific Review Group (SRG) composed primarily of non-Federal scientists who have expertise in relevant scientific disciplines and current research areas. The second level of review is performed by Institute and Center National Advisory Councils or Boards. Councils are composed of both scientific and lay members chosen for their expertise, interest, or activity in matters related to health and disease. Only applications that are favorably recommended by both the SRG and the Advisory Council may be recommended for funding. Information about the peer-review process can be found at *http://grants.nih.gov/grants/peer_review_process.htm* and at *http://public.csr.nih.gov.*

What is the total NIH budget? What is the budget for AIDS research?

The total Fiscal Year 2012 budget for the NIH is more than $31.2 billion to support medical research. More than 83 percent of the NIH's funding is distributed through almost 50,000 competitive grants to more than 300,000 researchers at some 3,000 universities, medical schools, and other research institutions in every state and around the world. About 10 percent of the NIH's budget supports projects conducted by scientists in NIH's own intramural laboratories, most of which are on the NIH campus in Bethesda, Maryland.

For information about the NIH budget, see: *http://officeofbudget.od.nih.gov.*

AIDS-related research represents approximately 10 percent of the total NIH research budget. The Fiscal Year 2012 appropriation for NIH AIDS research was $3.07 billion.

For information about the NIH AIDS research budget, see *http://www.oar.nih.gov/budget.*

What is the economic impact of NIH research investments?

The NIH is a catalyst and powerhouse for creating and maintaining economic growth across the United States. As documented by the United for Medical Research report, *An Economic Engine,* in 2010, NIH funding led to the creation of 487,900 jobs and produced $68.035 billion in new economic activity.

A published report, *Economic Impact of the Human Genome Project,* prepared by the Battelle Technology Partnership Practice, estimated that the initial Federal investment of $3.8 billion in the Human Genome Project produced a stunning $796 billion in economic benefits to the United States—a 141 to 1 return on investment. In 2010 alone, human genome sequencing activities generated $67 billion in U.S. economic output and 310,000 U.S. jobs.

NIH research and discoveries have led to dramatic growth in the field of medical innovation. These industries innovate and compete by leveraging NIH research and knowledge. As documented in *An Economic Engine,* the medical innovation sector employed almost 1 million people and paid total wages of $84 billion as of 2008, and exported $90 billion of goods and services in 2010.

For more information on the economic benefits of NIH research investments, see *http://www.nih.gov/about/director/10212011_advances.pdf.*

ABOUT NIH HIV/AIDS RESEARCH

Why is there still a need for AIDS research?

Significant progress has been made in HIV prevention and treatment, but many scientific challenges still lie ahead. The HIV/AIDS pandemic will remain the most serious public health crisis of our time until better, more effective, and affordable prevention and treatment regimens—and eventually a cure—are developed and universally available.

Today, the HIV/AIDS pandemic remains a global burden that affects people in every nation. The Joint United Nations Programme on HIV/AIDS (UNAIDS) reports that at the end of 2010, more than 34 million people were living with HIV worldwide, 2.7 million were newly infected, and 1.8 million people died of AIDS-related illnesses. AIDS also continues to be a major public health problem in the United States, with 50,000 estimated new infections annually. According to data from the Centers for Disease Control and Prevention, an estimated 1.2 million Americans are living with HIV, and 20 percent of them are unaware of their infection. AIDS disproportionately affects racial and ethnic populations, women of color, young adults, and men who have sex with men. Further research to improve prevention and treatment is urgently needed.

What are the major areas of NIH AIDS research?

The NIH supports a global and comprehensive AIDS research program—the largest and most significant public investment in AIDS research in the world. The major scientific areas of emphasis in the NIH AIDS research portfolio are:

Expanding Basic Discovery Research

- Etiology and Pathogenesis

Reducing New Infections

- Vaccines
- Microbicides
- Behavioral and Social Science
- Therapeutics as Prevention

Improving Disease Outcomes for HIV-Infected Individuals

- Drug Discovery, Development, and Treatment
- Research Toward a Cure

Reducing HIV-Related Disparities

- Training, Infrastructure, and Capacity Building

Translating Research From Bench to Bedside to Community

- Natural History and Epidemiology
- Information Dissemination

What are the NIH priorities in basic science/pathogenesis research?

Improving our understanding of the basic relationship between HIV/AIDS and the human immune system is the key to the discovery of new and improved treatments and methods for preventing HIV infection. Research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, methodologies for diagnosis of HIV infection, and tools for monitoring disease progression and the safety and effectiveness of antiviral therapies. Groundbreaking strides have been made toward understanding the fundamental steps in the life cycle of HIV, the host-virus interactions, and the clinical manifestations associated with HIV infection and AIDS.

However, important questions remain about the molecular interactions involved in the regulation of HIV expression and replication, why the host immune response is not fully effective in controlling HIV infection, and how reservoirs of infection persist in the body despite treatment. Understanding these basic science issues is critical to generating new treatment targets and

vaccine approaches; and to understanding how HIV viral reservoirs might one day be eliminated, opening the door to a possible cure.

The NIH is focusing efforts on research to:

- Further the understanding of the virus and how it causes disease, including studies to delineate how sex, gender, age, ethnicity, race, pregnancy, nutritional status, and other factors interact to influence vulnerability to infection and disease progression and affect treatment success or failure, including immune dysregulation and inflammation.
- Examine the genetic determinants associated with HIV susceptibility, disease progression, and treatment response that may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetic sequence.
- Examine the mechanisms by which HIV establishes and reactivates latent reservoirs of infection.
- Further understanding of factors associated with the ability of the host to restrict HIV infection and/or mitigate HIV disease progression. A better understanding of these processes could help identify key targets for the development of new therapeutic strategies to prevent or control HIV infection or possibly lead to a cure for HIV disease.
- Understand the application of genetics, genomics, epigenetics, proteomics, systems biology, and other related technologies to increase our knowledge of HIV/AIDS and the host immune response.
- Further understand the biology of HIV transmission, which will be of importance for all HIV prevention research.
- Better understand HIV coinfections (including tuberculosis and hepatitis C), comorbidities, and malignancies, as well as factors related to premature aging and cardiovascular, metabolic, neurologic, and other clinical complications.
- Better understand the differences in HIV transmission, treatment, and progression in women compared with men, as well as the unique clinical manifestations of HIV disease in women.

What are the NIH priorities in HIV prevention research?

The prevention of HIV infection is a key NIH research priority. Reducing HIV incidence will require a combination of various biomedical, behavioral, and structural interventions. Priorities for NIH-supported research include the development of vaccines, microbicides, and behavioral interventions to reduce HIV transmission; prevention of mother-to-child transmission; circumcision to prevent heterosexual HIV acquisition in men; and the use of antiretroviral therapy (ART) to prevent HIV infection. Strategies are particularly needed to address specific high-risk populations, including men who have sex with men (MSM), women, older individuals, and adolescents, particularly among racial and ethnic populations, and to develop prevention strategies that can be effectively utilized in low-resource settings.

NIH research priorities in the field of HIV prevention include:

Vaccine Research: Historically, vaccines have been our best weapon in the fight against humanity's worst infectious diseases, including smallpox and polio. The NIH supports a broad AIDS vaccine research portfolio encompassing basic, preclinical, and clinical HIV vaccine research. This includes fundamental research to better understand how HIV interacts with the human immune system; studies of improved animal models for the preclinical evaluation of vaccine candidates; testing the most promising vaccine candidates; and studies to identify and better understand potentially protective immune responses in HIV-infected individuals. Information gained from these studies is being used to inform the design and development of novel vaccine strategies. Since the announcement of the results of the RV144 trial in Thailand, that demonstrated for the first

time that a vaccine candidate could have a protective effect, the NIH has supported an unprecedented collaborative effort with investigators around the world to identify clues about the necessary immune responses required to protect against HIV acquisition.

Microbicides Research: A safe and effective microbicide may be the best hope for woman-controlled HIV prevention. Microbicides are antimicrobial agents and other products that could be applied topically and used alone or in combination with other strategies to prevent transmission of HIV and other sexually transmitted infections. The NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates. The NIH supports basic science aimed at understanding how HIV crosses mucosal membranes and infects cells; behavioral and social science research on adherence to, acceptability, and use of microbicides among different populations; studies of the safety of microbicide use during pregnancy and menopause; studies in adolescents, and in MSM; and implementation research to better understand how to integrate a potential product into community prevention practices. Basic science and clinical studies have shown promise for the use of antiretroviral (ARV)-based microbicides as HIV prevention strategies. Follow-up studies testing different ARV- and non-ARV-based products are underway or being developed. The NIH also is researching topical microbicides that can be applied rectally to prevent HIV infection among MSM.

Therapeutics as Prevention: A critical area of prevention research is the study of the use of antiretroviral therapies to prevent new infections. Focal points for NIH research include:

- **Prevention of Mother-to-Child HIV Transmission:** The NIH pioneered research demonstrating the dramatic reduction in risk of HIV transmission from mother to child as a result of the administration of ART to both an HIV-infected pregnant woman and to her infant. As a result of that NIH-supported research, fewer than 200 HIV-infected babies were born in the United States last year. The NIH is supporting research on new multidrug ARV regimens for the prevention of HIV mother-to-child-transmission during pregnancy and breastfeeding that can be implemented in resource-constrained settings.
- **Treatment as Prevention:** The NIH-supported HPTN 052 study demonstrated that early initiation of ARV treatment for HIV-infected heterosexual individuals resulted in a 96 percent reduction in sexual transmission of HIV to their uninfected partners. The research was named the 2011 Breakthrough of the Year by the journal *Science*. Additional information about HPTN 052 is available at *http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HPTN052.aspx*.
- **Pre-Exposure Prophylaxis (PrEP):** A major NIH-sponsored clinical trial (iPrEx) demonstrated that use of an ARV drug by some high-risk uninfected MSM could reduce their risk of acquiring HIV. The NIH is continuing to examine strategies providing ARV medicines to people who are not infected with HIV but who are at high risk of becoming infected, including testing PrEP in high-risk, uninfected women and adolescents.
- **Test and Treat:** The NIH supports research into a potential innovative prevention strategy known as "test and treat," designed to determine whether a communitywide HIV testing and counseling program with immediate treatment for HIV-infected individuals can decrease the overall rate of new HIV infections in that community.

Circumcision: NIH-supported researchers in Kenya and Uganda demonstrated that medically performed circumcision significantly reduces a man's risk of acquiring HIV through heterosexual intercourse. The trial in Kenya showed a 53 percent reduction of HIV acquisition in circumcised men relative to uncircumcised men, while a trial in Uganda showed that HIV acquisition was reduced by 48 percent in circumcised men.

Additional information about the studies can be found at *http://www.niaid.nih.gov/news/newsreleases/2006/Pages/AMC12_06press.aspx*. Adult male circumcision is being implemented internationally as part of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

Behavioral interventions: The NIH supports research to better understand how to change the risk behaviors that lead to HIV infection and disease progression; maintain protective behaviors once they are adopted; and improve our understanding of the environmental, social, and cultural factors associated with HIV infection and disease outcomes, including stigma. Determining effective strategies to test HIV-infected persons, link them to care, and to promote adherence to ART is another important area of NIH-supported research. Studies are developing and evaluating interventions directly targeted to substance abuse and sexual behaviors associated with HIV transmission.

Combination Prevention Strategies: The NIH is conducting studies integrating behavioral and social science methods with biomedical prevention strategies and community-based approaches to engaging and retaining persons in care in order to improve care and reduce HIV transmission. The NIH also supports research initiatives to better understand the multiple factors related to adherence, using novel ways to ensure that patients take their medications and use prevention strategies appropriately.

What are the NIH priorities in HIV treatment research?

NIH research has established the scientific basis for, and extensively assessed the best uses of, HIV therapies that have saved more than 14 million years of life around the world (*http://sti.bmj.com/content/86/Suppl_2/ii67.full*). Currently, there are more than 30 U.S. Food and Drug Administration-approved antiretroviral (ARV) drugs available to people infected with HIV. The use of these drugs in combination treatment regimens has transformed HIV infection from a rapidly and uniformly fatal illness to one that can be successfully managed with appropriate care and monitoring. While antiretroviral therapy (ART) has enabled people infected with HIV to lead longer and healthier lives, drug resistance, tolerability, and toxicity issues remain. Recent epidemiologic studies have shown that the incidence of coinfections, comorbidities, AIDS-defining and non-AIDS-defining malignancies, and complications associated with long-term HIV disease and ART are increasing.

The NIH supports a comprehensive therapeutics research program to discover new, less toxic, and more effective therapies, drug classes, and combinations to:

- Treat HIV and the comorbidities associated with long-term HIV disease and ARV treatment such as malignancies; cardiovascular diseases; and metabolic, neurologic, and neurocognitive disorders; and other conditions associated with aging.
- Prevent and treat AIDS-related coinfections such as hepatitis, malaria, and tuberculosis
- Overcome drug resistance and treatment failure
- Address new viral and cellular drug targets—including therapies targeting HIV integrase, various steps in the virus entry process, and virion maturation.

NIH research on AIDS therapeutics also seeks to:

- Develop drugs and treatment strategies for HIV and its complications that are easier to use and less toxic, and can be made readily accessible in resource-limited settings
- Understand how genetic determinants, sex, gender, race, age, nutritional status, treatment during pregnancy, and other factors interact to affect treatment success or failure
- Improve therapeutic options for HIV-infected children, adolescents, and women
- Discover the next generation of drugs that may be used in potential "treatment as prevention" strategies
- Design, develop, and test strategies to eradicate persistent viral reservoirs that may lead to a potential or functional cure for HIV disease
- Examine the possible applications of customized therapeutic and preventive regimens formulated based on a patient's genetic sequence.

What are the NIH priorities in HIV cure research?

Although antiretroviral therapy enables many people infected with HIV to effectively control their virus levels and stay relatively healthy, some virus remains hidden in a latent or persistent form in cells and tissues where it is not susceptible to antiretrovirals. The FY 2013 Trans-NIH AIDS Strategic Plan includes a section devoted to research toward a cure. The NIH supports and is an active participant in the international process to develop a strategy "Towards an HIV Cure," which is being launched in conjunction with the *XIX International AIDS Conference (AIDS 2012)*.

The NIH is supporting basic and clinical research to:

- Understand viral reservoirs, viral latency, and viral persistence, including research on how HIV integrates into the host genome; genetic factors associated with reactivation of the virus; and other barriers to HIV eradication.
- Identify and test various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.
- Develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system.
- Evaluate lead compounds, drug regimens, and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.
- Design and test vaccines that would be capable of suppressing viral replication and preventing disease progression.
- Develop and test strategies to maintain adherence/compliance to reduce the risk of developing drug resistance and the establishment of viral reservoirs.

In addition, the National Institute of Allergy and Infectious Diseases (NIAID) launched the Martin Delaney Collaboratory: Towards An HIV-1 Cure (U19), a funding initiative designed to foster public-private partnerships to accelerate progress toward an HIV cure named in memory of the longtime AIDS activist and founder of Project Inform. NIAID announced the award of grants to three research teams focused on developing strategies that could help to rid the body of HIV. Each research team will pursue a unique and complementary approach aimed at eradicating reservoirs of HIV infection.

What are the NIH priorities in translational/implementation research?

The NIH supports an extensive range of translational/implementation research that addresses the feasibility, effectiveness, and sustainability required for the scale-up and implementation of interventions in "real world" settings. The NIH supports:

Translational Research: including critical epidemiologic and natural history studies, collaborative networks, and specimen repositories to evaluate various operational strategies to scale up and evaluate treatment programs and successful prevention interventions in communities at risk.

Natural History and Epidemiology Research: in domestic and international settings to monitor epidemic trends, develop and evaluate HIV prevention modalities, track the changing clinical manifestations of HIV disease in different populations, and measure the effects of treatment regimens.

Research in Critical Populations: including high-priority epidemiology studies of groups and populations affected by HIV and at high risk for infection in the United States and around the world, such as individuals aged 50 and older, men who have sex with men, substance users, women, and adolescents, especially African American and Hispanic adolescents. This research includes studies on the mechanisms of disease progression; the role of race and gender; the effects of increased HIV testing and linkage to care; and implementation/operational science, including the evaluation of strategies to scale up efficacious and cost-effective interventions at the community level.

Research to Reduce HIV-Related Disparities: including research to better understand the causes of HIV-related health disparities, their role in disease transmission and acquisition, and their impact on treatment access and

effectiveness. These include disparities among racial and ethnic populations in the United States, between developed and resource-constrained nations, between men and women, between youth and older individuals, and disparities based on sexual identity. The NIH supports research training for new investigators from racial and ethnic communities, development of research infrastructure, community outreach, information dissemination, and research collaborations to help reduce health disparities.

Information Dissemination: effective information dissemination as an integral component of HIV prevention and treatment efforts. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to rapidly translate research results into practice and to shape future research directions. The NIH supports initiatives to facilitate the dissemination of research findings; and enhance recruitment and retention of volunteers in clinical studies, including women, adolescents, and racial and ethnic populations. The NIH supports a process to develop and continually update Federal state-of-the-art guidelines on the use of antiretroviral therapy and for the management of HIV complications for adults and children. These guidelines are disseminated to health care providers and patients through the *AIDSinfo* Web site and the Spanish language site *infoSIDA*.

What is the NIH Office of AIDS Research (OAR)?

The Office of AIDS Research (OAR), established in 1988, has unique legislative authorities unlike any other NIH entity to plan, coordinate, evaluate, and budget the entire $3 billion NIH AIDS research program, which represents approximately 10 percent of the total NIH budget—the largest and most significant public investment in AIDS research in the world. OAR serves as a model of trans-NIH planning and management, operating as an "Institute without walls," vested with primary responsibility for overseeing all NIH AIDS-related research, and thus allowing the NIH to pursue a united research front against the global AIDS epidemic.

Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of every Institute and Center of the NIH. This diverse research portfolio demands an unprecedented level of trans-NIH scientific coordination and management of research funds. OAR coordinates the scientific, budgetary, legislative, and policy elements of the NIH AIDS research portfolio and sets the trans-NIH scientific priorities for this large and diverse program. Using its legislative authorities, OAR has established comprehensive trans-NIH planning, budgeting, and portfolio analysis processes to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively and efficiently.

OAR identifies emerging scientific opportunities and public health challenges that require focused attention, manages and facilitates multi-Institute and trans-Institute activities to address those needs, fosters research by designating funds and supplements funds to jump-start or pilot program areas, sponsors reviews or evaluations of research program areas, and facilitates the support of international AIDS research and training. OAR also supports a number of initiatives to enhance dissemination of research findings to researchers, physicians, institutions, communities, constituency groups, and patients.

What is the NIH AIDS research budget?

The FY 2012 (October 1, 2011–September 30, 2012) appropriation for HIV/AIDS research is $3.07 billion. This budget includes the total trans-NIH support for intramural and extramural research for basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the wide spectrum of AIDS-associated malignancies, opportunistic infections, coinfections, and clinical complications; as well as research management support, research centers, and training.

Is the NIH involved in international AIDS research activities or programs?

Yes. Research to address the global pandemic is essential. Since the early days of the epidemic, the NIH has maintained a strong international AIDS research portfolio that has grown to include projects in approximately 100 countries around the world. NIH AIDS research studies are designed so that the results are relevant for both the host nation and the United States. These research programs also enhance research infrastructure and training of in-country scientists and health care providers. New collaborations have been designed to improve medical and nursing education as a mechanism to build a cadre of global health leaders. Most of these grants and contracts are awarded to U.S.-based investigators to conduct research in collaboration with in-country scientists; some are awarded directly to investigators in international scientific or medical institutions. This research includes efforts to develop HIV vaccine and microbicide candidates, behavioral prevention research, strategies to prevent mother-to-child transmission, and approaches to using antiretroviral therapy in resource-poor settings.

How is NIH research addressing the AIDS epidemic in the United States?

NIH research is addressing the need for comprehensive strategies to decrease HIV transmission and to improve treatment options and treatment outcomes in affected, vulnerable populations, including women, racial and ethnic populations, men who have sex with men, drug users, young people, and aging populations in the United States. These interventions address issues such as the co-occurrence of other sexually transmitted infections, hepatitis, drug abuse, and mental illness; and consider the role of culture, family, and other social factors in the transmission and prevention of these disorders. The Trans-NIH AIDS Strategic Plan includes a section devoted to the research needs and priorities to address HIV/AIDS in racial and ethnic populations of the United States. NIH-funded programs have increased the number of training positions for AIDS-related research, including programs specifically designed to recruit individuals from underrepresented populations into research careers and to build research infrastructure at minority-serving institutions in the United States.

In July 2010, the Administration released the first comprehensive National HIV/AIDS Strategy (NHAS) for the United States. Senior NIH officials are involved in the Federal interagency working group that continues to work with the White House to implement the NHAS. The NHAS focuses on reducing the number of new HIV infections, increasing access to care for people living with HIV and improving disease outcomes, reducing HIV-related health disparities, and achieving a more coordinated national response. NIH research provides the scientific foundation to support the goals of the NHAS.

How is NIH AIDS research addressing the needs of women?

Women represent one-half of global HIV cases, and more than 60 percent of the epidemic in some sub-Saharan African countries. One in four people living with HIV infection in the United States is female. Two-thirds of HIV-infected women in the United States are African American; 15 percent are Hispanic/Latina. The NIH-sponsored HPTN 064 (ISIS) study found that HIV seroincidence in some communities of African American women is similar to women in some African countries. HIV-infected African American women have twice the risk of dying from AIDS compared with their white counterparts.

The NIH is committed to improving our understanding of the epidemic in women and girls and developing interventions to decrease their vulnerability to HIV and improve treatment and prevention outcomes. Approximately 46 percent of participants in NIH-funded clinical trials are female. NIH-supported research, including studies through the Microbicide Trials Network (MTN), International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group, AIDS Clinical Trials Group (ACTG), Adolescent Medicine Trials Network (ATN), and HIV Prevention Trials Network (HPTN) have been critical to advancing understanding of:

- Differences in HIV vulnerability and in the development of HIV disease between women and men

- Metabolic issues and antiretroviral side effects in women
- Female genital tract microbiology and immunity and its impact on HIV risk and protection
- The impact of HIV on maternal health, pregnancy, and breastfeeding
- Strategies to prevent mother-to-child HIV transmission
- Social determinants of HIV risk—including violence, substance use, and poverty
- Oral and topical biomedical prevention in women including during pregnancy, adolescence, and menopause.

The Trans-NIH AIDS Strategic Plan contains a section devoted to research on women and girls. Current NIH research priorities include studies to:

- Identify the biological, behavioral, social, and economic factors related to vulnerability to infection for women and girls, including issues related to drug use, stigma, and domestic violence
- Better understand the factors that influence HIV transmission and pathogenesis, responses to HIV treatment, and the unique clinical complications of HIV in women and girls
- Define and analyze the impact of aging on HIV risk, pathogenesis, and prevention in women compared with men
- Develop and study interventions to prevent intra-partum and breastfeeding-related mother-to-child HIV transmission.

What are clinical trials, and where can I find detailed information about them?

HIV/AIDS clinical trials are research studies in which new therapies and prevention strategies for HIV infection and AIDS are tested in humans. Carefully conducted clinical trials are the fastest and safest way to help find treatments and prevention strategies that work. New therapies are tested in humans only after laboratory and animal studies show promising results.

- In Phase I clinical trials, the experimental therapies are given to small numbers of people to help determine safe doses.
- Larger groups of patients may then receive the therapies in Phase II trials to help measure side effects and preliminary effectiveness.
- The treatments may then be used in even larger Phase III studies to compare the new treatment with ones already in use or to help estimate other effects of the drug.

The NIH supports a comprehensive portfolio of clinical research on HIV infection, including both intramural and extramural clinical trials, cohort-based studies, and research consortia and collaborations. These studies are conducted in the United States and at international sites.

Clinical trial volunteers make invaluable contributions to the scientific understanding of HIV and AIDS and to the development and improvement of therapeutic and prevention approaches to help reduce the pandemic. In 2011, more than 100,000 volunteers participated in studies through NIH-funded domestic and international clinical trials networks and cohort studies. Approximately 46 percent of those participants were female. Volunteers who participate in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and make a vital contribution to medical research.

How can I find more information about HIV/AIDS clinical trials?

AIDSinfo provides free, up-to-date information on clinical trials evaluating experimental HIV/AIDS drugs, microbicides, and vaccines. Information also is available at 1-800-HIV-0440 (1-800-448-0440) in the United States, or 1-301-519-0459 for international callers.

The National Library of Medicine offers online access to information on HIV/AIDS clinical trials through the *ClinicalTrials.gov* database.

For information about clinical trials in the NIH Intramural Research Program, visit *http://irp.nih.gov/our-research/scientific-focus-areas/clinical-research.*

The National Institute of Allergy and Infectious Diseases sponsors the "Be The Generation To End the AIDS Epidemic" initiative to promote awareness, understanding, dialogue, and support for biomedical prevention research, including HIV vaccines, microbicides, and pre-exposure prophylaxis. For information, visit *http://bethegeneration.nih.gov.*

For additional information about clinical trials in general, visit the NIH Clinical Research Trials and You Web site (*http://www.nih.gov/health/clinicaltrials*), an NIH resource that catalogs and explains thousands of ongoing clinical studies.

What are the Federal HIV treatment guidelines?

The NIH manages a process to develop U.S. Department of Health and Human Services guidelines to help physicians in the medical management of HIV infection and issues surrounding HIV infection. Separate guidelines have been developed for:

- Treatment of adults and adolescents
- Treatment of children
- Treatment of pregnant women and prevention of mother-to-child transmission of HIV
- Prevention and treatment of opportunistic infections in children
- Prevention and treatment of opportunistic infections in adults

Federal HIV treatment guidelines are written, reviewed, and updated by panels of HIV experts from across the country. Panel members include physicians, pharmacists, researchers, and HIV treatment advocates.

Topics covered in the guidelines include:

- Goals of HIV treatment
- When to start treatment
- Monitoring patient health
- Anti-HIV medication side effects and their management
- Anti-HIV medications for use during pregnancy
- Diagnosis of HIV infection in infants.

The guidelines are distributed widely through *AIDSinfo* and the Spanish-language equivalent site, *infoSIDA*. Those sites also include information about Food and Drug Administration-approved and investigational HIV/AIDS drugs, clinical trials information, educational information, a variety of mobile resources and tools, and a searchable HIV/AIDS glossary. You can join the *AIDSinfo* E-News listserv (*http://aidsinfo.nih.gov/other/subscribe.aspx)* to receive an e-mail notification when updated guidelines are released.

Although Federal treatment guidelines are written in sophisticated medical language, a series of easy-to-read fact sheets based on the Federal guidelines, "HIV and Its Treatment: What You Should Know," are available at *http://aidsinfo.nih.gov/other/factsheet.aspx.*

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